

# INTERNATIONAL SEARCH REPORT

International application No.

PCT/US04/14540

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12Q 1/68; A01N 43/04; C07H 21/04; A61K 31/07  
US CL : 435/6, 91.1, 325, 375; 536/23.1, 24.3, 24.33, 24.5, 514/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
U.S. : 435/6, 91.1, 325, 375; 536/23.1, 24.3, 24.33, 24.5, 514/44

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
Please See Continuation Sheet

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
A	BRANCH, AD. A good antisense molecule is hard to find. TIBS, 1998 Vol. 23:45-50, see entire article.	26-28, 32-36, and 43-49
A	JEN et al. Suppression of gene expression by targeted disruption of messenger RNA: Available options and current strategies. Stem Cells, 2000 Vol. 18:307-319, see entire article.	26-28, 32-36, and 43-49
X	MORISHITA et al. Novel therapeutic strategy for atherosclerosis ribozyme oligonucleotides against apolipoprotein(a) selectively inhibits apolipoprotein (a) but not plasminogen gene expression. Circulation, 1998 Vol. 98:1898-1904, see page 1899, first column.	18, 26, 27, 31, 34, 35, 37, 47-49
X	MCLEAN et al. cDNA sequence of human apolipoprotein(a) is homologous to plasminogen. Nature, 1997 Vol. 330:132-137, see Figure 1b at dotted underline.	18, 26, 27, 31, 34, 35, 37, 47-49
X	US 6,008,344 (BENNETT et al.) 23 February 1999 (23.2.1999), see SEQ ID NO:43	18, 20-27, 31, 34-40, and 47-49
X	WO 99/35241 (PHARMACEUTICALS, INC.) 8 January 1998 (8.1.1999), see page 23, first full paragraph	18, 22-25, and 31



Further documents are listed in the continuation of Box C.



See patent family annex.

* Special categories of cited documents:		"T"	later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention
"A"	document defining the general state of the art which is not considered to be of particular relevance	"X"	document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone
"E"	earlier application or patent published on or after the international filing date	"Y"	document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art
"L"	document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)	"&"	document member of the same patent family
"O"	document referring to an oral disclosure, use, exhibition or other means		
"P"	document published prior to the international filing date but later than the priority date claimed		

Date of the actual completion of the international search

06 December 2005 (06.12.2005)

Date of mailing of the international search report

25 JAN 2006

Name and mailing address of the ISA/US

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## Box No. I Nucleotide and/or amino acid sequence(s) (Continuation of item 1.b of the first sheet)

1. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, the international search was carried out on the basis of:

a. type of material



a sequence listing



table(s) related to the sequence listing

b. format of material



on paper



in electronic form

c. time of filing/furnishing



contained in the international application as filed



filed together with the international application in electronic form



furnished subsequently to this Authority for the purposes of search

2. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

3. Additional comments:

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## Box No. II Observations where certain claims were found unsearchable (Continuation of item 2 of first sheet)

This international search report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:
3. ☐ Claims Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box No. III Observations where unity of invention is lacking (Continuation of item 3 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  2. ☐ As all searchable claims could be searched without effort justifying additional fees, this Authority did not invite payment of any additional fees.
  3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  4. ☒ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.: 1-28, 30-49, and SEQ ID NO:85
- Remark on Protest**
- ☐ The additional search fees were accompanied by the applicant's protest and, where applicable, the payment of a protest fee.
- ☐ The additional search fees were accompanied by the applicant's protest but the applicable protest fee was not paid within the time limit specified in the invitation.
- ☐ No protest accompanied the payment of additional search fees.

**BOX III. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING**

Group I, claims 1-28 and 31-49 drawn to compound targeted to apolipoprotein (a), wherein said compound inhibits the expression of apolipoprotein (a) and a method of using said compound in cells or tissues comprising administering a compound targeted to apolipoprotein (a), wherein said compound inhibits the expression of apolipoprotein (a) or treating a disease or disorder associated with apolipoprotein (a) comprising administering a compound targeted to apolipoprotein (a), wherein said compound inhibits the expression of apolipoprotein (a).

Group II, claim 29, drawn to a method of screening for a modulator of apolipoprotein (a).

Group III, claim 30, drawn to a diagnostic method for identifying a disease state.

The inventions listed as Groups I-III do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

Groups II and III are each directed to different methods than the treatment methods in Group I. Methods of screening and methods of identifying are clearly different special technical features from the methods of treatment.

Claims 1, 19, and 28 are subject to an additional restriction since it is not considered to be a proper genus/Markush. If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner must examine all the members of the Markush group in the claim on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction. Broadly, unity of invention exists where compounds included within a Markush group (1) share a common utility, and (2) share a substantial structural feature disclosed as being essential to that utility.

Claims 1, 19, and 28 specifically claims antisense SEQ ID NOs. 85-96, 11, 23, 28, 30, 31, 33-36, 39, 42, 43, and 45, which are targeted to and modulate the expression of apolipoprotein (a). Although the antisense sequences claimed each target and modulate expression of apolipoprotein (a), the instant antisense sequences are considered to be unrelated, since each antisense sequence claimed is structurally and functionally independent and distinct for the following reasons: each antisense sequence has a unique nucleotide sequence, each antisense sequence targets a different and specific region of apolipoprotein (a) nucleic acid, and each antisense, upon binding to a apolipoprotein (a) nucleic acid, functionally modulates (increases or decreases) the expression of the gene and to varying degree (per applicants' Table 1 in the specification). As such, the Markush/genus of antisense sequences in claims 1, 19, and 28 is not considered to constitute a proper genus, and is therefore subject to restriction. Furthermore, a search of more than one (1) of the antisense sequences claimed in claims 1, 19, and 28 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one (1) of the claimed antisense sequences. In view of the foregoing, one (1) antisense sequence is considered to be a reasonable number of sequences for examination. Accordingly, applicants are required to elect one (1) antisense sequence from claims 1, 19, and 28. Note that this is not a species election.

Applicants will obtain a search of the first invention listed in the first group. For every other invention applicants wish to have searched, applicants need to elect the group and pay an additional fee. Additionally, applicants will obtain a search of the first sequence listed in

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the first invention. For every other sequence applicants wish to have searched, applicants need to elect the sequence and pay an additional fee.

Continuation of B. FIELDS SEARCHED Item 3:  
STN, WEST, NPL, Medline, CaPLUS, EmBase  
search terms: antisense, ribozyme, apolipoprotein (a), plasminogen